

TABLE A16.—*Experiments concerning the effect of the inhalation of cigarette smoke or its constituents upon the respiratory tract of animals (cont.)*
(Figures in parentheses represent total number survivors in specific group)

Author, year, country, reference	Animal and strain	A. Type of exposure B. Duration C. Material	Results			Comments
Dontenwill and Wiebecke, 1966, Germany (77).	Golden hamsters. C. — E. 320	A. Chamber. B. Up to 4 cigarettes per day for up to 2 years. C. Cigarette smoke.	<i>Number of animals dead at 540 days</i>	<i>Daily average exposure (cigarettes)</i>	<i>Histologic findings in dead animals</i>	MET des = desquama- tive metaplasia. MET bronch = bron- chial papillary metaplasia. PAP trach = tracheal papillomata or intense tracheal metaplasia.
			40	1	8/ 40 MET des	
			40	2	8/ 40 MET des	
			80	1-2	44/ 80 MET des (3 MET bronch, 2 PAP trach)	
			143	1-4	67/143 MET des (13 MET bronch, 8 PAP trach)	
Leuchtenberger and Leuchten- berger 1966, Switzerland (164).	CF ₁ mice.	A. Chamber. B. Up to 1,000 hours. C. Cigarette smoke, exposure to in- fluenza virus (PR8).	<i>Marked squamous cell metaplasia (percent)</i>	<i>Marked dysplasia (percent)</i>	<i>Marked transgression of lung parenchyma (percent)</i>	†Epithelial tissues of these animals showed an increased frequency of cellular atypism. The authors concluded that PR8 influenza virus may act as a cofactor in malig- nant transformation.
		Controls (100):				
		Male	—	—	—	
		Female	—	—	—	
		Smoke exposed (59):				
		Male	—	6.0	3.0	
		Female	—	—	—	
		Virus exposed (59):				
		Male	11.0	21.0	13.0	
		Female	—	—	5.0	
		Smoke and virus exposed (68):				
		Male	9.0	43.0	†18.0	
		Female	29.0	54.0	†33.0	

TABLE A16.—*Experiments concerning the effect of the inhalation of cigarette smoke or its constituents upon the respiratory tract of animals (cont.)*
(Figures in parentheses represent total number survivors in specific group)

Author, year, country, reference	Animal and strain	A. Type of exposure B. Duration C. Material	Results					Comments	
Rockey and Speer, 1966, U.S.A. (223).	Mongrel dogs: C. 11. E. 19.	A. Tracheal fenestra- tion (10).						†Carcinoma <i>in situ</i> noted in 5 separate sites in this animal.	
		Nostril inhala- tion (9).							
		B. Tracheal fenestra- tion—284 treat- ment days.	Controls (11)	9	1	1	0		0
		Nostril inhalation— 180 treatment days.	Tracheal fenestra- tion (10)	10	5	6	1		†1
		C. Cigarette smoke.	Nostril in- halation (9)	6	0	0	0		0
Auerbach et al., 1967, U.S.A. (10).	Beagle dogs: C. 10 (2 with tracheostoma). E. 10.	A. Tracheostoma.	Controls, experimental: No histologic change in bronchial epithelium: a. 1 animal died at 24 days and no histologic change noted. b. 5 animals sacrificed at 421 days and nuclear atypism noted in all. c. 2 animals died at 229 and 278 days and nuclear atypism was noted but of lesser severity than in those sacrificed at 421 days.						
		B. Up to 12 cigarettes per day for up to 421 days.							
		C. Cigarette smoke.							
Harris and Negroni, 1967, England (121).	C57BL mice: C. 200. E. 1,437.	A. Chamber.						This strain of mice is noted for its lack of spontaneous lung tumor formation. Animals exposed to cigarette smoke showed no hyper- plastic epithelial changes such as those noted by Leuchtenberger.	
		B. Smoke—12 ciga- rettes per 20 mice for 12 minutes every other day for lifetime.	<i>Treatment</i>	<i>Number</i>	<i>Number of lung carcinomas</i>				
		Controls	200	0					
		Influenza aerosol alone	682	15					
		Benzpyrene aerosol (4 exposures)	200	2					
		Smoking	200	8 (all adeno- carcinomas)					
		Influenza and benzpyrene	200	3					
		Influenza and smoking	155	3					

TABLE A16.—*Experiments concerning the effect of the inhalation of cigarette smoke or its constituents upon the respiratory tract of animals (cont.)*
(Figures in parentheses represent total number survivors in specific group)

Author, year, country, reference	Animal and strain	A. Type of exposure B. Duration C. Material	Results	Comments
Wynder et al., 1968, U.S.A. (327).	Male C57BL6 mice; C. and E.— more than 40.	A. Chamber. B. Up to 315 cigarettes. C. Cigarette smoke, nitrogen dioxide, volatile acids and aldehydes found in ciga- rette smoke, swine influenza virus.	Conclusions:† No squamous cell respiratory cancer noted. This is attributed to the limitation of inhalation time (CO and nicotine acute effects) and to the anatomically and physiologically intricate nasal passage defense system. Exposure to cigarette smoke, NO ₂ , or volatile acids and alde- hydes leads to reactive hyperplasia and metaplasia, both of which were noted to be reversible. Swine influenza virus exposure produced hyperplastic and metaplastic effects which could not be enhanced by subse- quent exposure to cigarette smoke.	†Results not provided in tabular form.
Laskin et al., 1970, U.S.A. (159).	Rats: C. 45. E. 3.	A. Chamber. B. 1 hour per day for up to 690 days. C. Benzo(a)pyrene aerosol, SO ₂ atmosphere (3.5 p.p.m.).	Exposure Atmosphere controls 3 Atmosphere plus benzo(a)- pyrene exposure 21 SO ₂ controls 3 SO ₂ plus benzo(a)- pyrene exposure 21	<i>Squamous cell carcinomas</i> 0/ 3 2/21 0/ 3 5/21
Hammond et al., 1970, U.S.A. (119).	Beagle dogs.	See text	See text.	

TABLE A21.—Outline of retrospective studies of tobacco use and cancer of the larynx

Author, year, country, reference	Sex	Number	Cases	Number	Controls	Collection of data
			Method of selection		Method of selection	
Schrek et al., 1950, U.S.A. (246).	M.	73	Referrals from V.A. hospitals in "entire midwest" to V.A. Cancer Center, Hines, Illinois, during 1942-44; patients with larynx-pharynx tumors clinically or histologically diagnosed:	522	From same set of referrals, patients with tumors other than lip, lung, larynx-pharynx:	Random sample of 5,003 admissions; questionnaires from Hines referrals for 1942-44; records included smoking history.
			<i>Percent</i>		<i>Percent</i>	
			Nonsmokers		Nonsmokers	
			Cigarettes		Cigarettes	
			Cigars		Cigars	
			Pipes		Pipes	
Valko, 1952, Czechoslovakia (292).	M-F	226	Clinic patients with cancer of the larynx:	108	Clinic patients of same age group with other diagnoses:	Medical history and questionnaire in clinic.
			<i>Percent</i>		<i>Percent</i>	
			Nonsmokers		Nonsmokers	
			Cigarettes			
			Cigars			
			Pipes			
Sadowsky et al., 1953, U.S.A. (232).	M.	273	White male admissions to hospitals in New York City, Missouri, New Orleans, Chicago; patients with diagnosed laryngeal tumors, 1938-43:	615	From same set of admissions, patients with illnesses other than cancer:	Sample of 2,605 out of 2,847 interviews (including smoking history) by trained lay interviewers.
			<i>Percent</i>		<i>Percent</i>	
			Nonsmokers		Nonsmokers	
			Cigarettes only		Cigarettes only	
			Cigars only		Cigars only	
			Pipe only		Pipe only	
			Some combination		Some combination	

TABLE A21.—Outline of retrospective studies of tobacco use and cancer of the larynx (cont.)

Author, year, country, reference	Sex	Cases		Controls		Collection of data
		Number	Method of selection	Number	Method of selection	
Blümlein, 1955, Germany (26).	M.	241	Clinic patients with cancer of larynx:	200	Patients with no laryngeal disease:	Personal history taken in clinic. Patients and controls over 40 years of age.
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Heavy smokers		Heavy smokers	
Wynder et al., 1956, U.S.A. (312).	M.	209	White male inpatients Memorial Cancer Research Center during 1952 to 1954, with benign or malignant epidermoid tumors of larynx:	209	Patients with other than epidermoid cancer, individually matched controls in same institutions:	Trained lay interviewers.
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Cigarettes		Cigarettes	
			Cigars		Cigars	
			Pipes		Pipes	
			Cigars/pipes		Cigars/pipes	
Wynder et al., 1956, India (312).	M.	132	Laryngeal cancer patients at Tata Memorial Hospital, 1952-54:	132	Controls individually matched as for U.S.A. data above:	Interviews for smoking and medical histories.
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Bidis		Bidis	
			Cigarettes		Cigarettes	
			Hookah		Hookah	
			Chilum		Chilum	
Schwartz et al., 1957, France (248).	M.	121	Patients hospitalized from 1954 through 1956 with laryngeal cancer, in Paris and other large cities:	242	Same time and sources; patients hospitalized for non-cancerous conditions or trauma:	Cases and controls individually matched within institutions; each member of a set questioned by the same trained lay interviewer.
			Percent		Percent	
			Smokers		Smokers ($p<0.05$)	
			Inhalers		Inhalers ($p<0.05$)	
			Roll their own cigarettes		Roll their own cigarettes	

TABLE A21.—Outline of retrospective studies of tobacco use and cancer of the larynx (cont.)

Author, year, country, reference	Cases			Controls			Collection of data
	Sex	Number	Method of selection	Number	Method of selection		
Wynder et al., 1957, Sweden (322).	M.	60	Patients at Radiumhemmet with squamous-cell cancer of larynx, from 1952 through 1955:	271	Patients from same source and time, with cancer other than squamous-cell of larynx:	By trained lay interviewers in hospital.	
			Percent		Percent		
			Nonsmokers	5	Nonsmokers		24
			Cigarettes	47	Cigarettes		36
			Cigars	17	Cigars		9
			Pipes	15	Pipes		16
		Mixed	17	Mixed	13		
Wynder et al., 1958, Cuba (325).	M.	142	Clinic patients in Havana during 1956-57, with histologically diagnosed epidermoid cancer of larynx.	220	Same source and time; apparently patients with cancers other than larynx, lung, or oral cavity, matched for age:	Interview of patients in clinic.	
	F.	32		214			
			Percent		Percent		
			Male Female		Male Female		
			Nonsmokers	1 13	Nonsmokers		16 66
			Cigarettes	62 72	Cigarettes		45 27
		Cigars	20 6	Cigars	22 6		
		Pipes	1 ..	Pipes	1 ..		
		Mixed	16 9	Mixed	16 ..		
Dutta-Choudhuri et al., 1959, India (86).	M-F	582	Patients in Calcutta cancer hospital during 1950-54, with laryngeal tumor diagnosed and confirmed by biopsy or smear:	288	Not specified	Tobacco histories obtained during 1951-54, apparently by interviewer.	
			Percent		Percent		
			Nonusers	14.1	Nonusers		41.7
			Cigarettes or bidi	77.8	Cigarettes or bidi		52.1
			Chew	3.1	Chew		3.8
			Both	5.0	Both		2.4

TABLE A21.—Outline of retrospective studies of tobacco use and cancer of the larynx (cont.)

Author, year, country, reference	Cases			Controls		Collection of data
	Sex	Number	Method of selection	Number	Method of selection	
Staszewski, 1960, Poland (259).	M.	207	Patients admitted to chronic disease hos- pital during 1957 and 1958 with histo- logically confirmed squamous-cell car- cinoma of the larynx:	912	Patients admitted during 1957 and 1958 to chronic disease center for cancer- ous and noncancerous conditions pre- sumably not related to tobacco con- sumption:	Author interviewed pa- tients suspected of lung cancer for smoking history and background.
	F.	13		1,813		
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Cigarettes only		Cigarettes only	
			Pipes and/or cigars		Pipes and/or cigars	
			"Heavy smokers"		"Heavy smokers"	
			Inhalers		Inhalers	
			Female smokers		Female smokers	
Rozenbils, 1967, Australia (229).	M.	191	Patients admitted to 3 major hospitals with cancer of larynx and hypopharynx:	No controls.		Patient interviews.
	F.	21				
			Percent			
			Nonsmokers			
			Smokers			
			Heavy smokers			
Terracol et al., 1967, France (274).	M.	961	Private service and clinic patients of ENT hospital:	No controls.		Patient interviews.
			Percent			
			Nonsmokers			
			Smokers			
Svoboda, 1968, Czechoslovakia (271).	M.	205	Patients admitted to a regional hospital over a period of 6 years all confirmed histologically:	320	Male controls	Cases: patient interviews. Controls: not stated.
	F.	10				
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Cigarettes		Cigarettes (approximately) ..	
			Pipes		Pipes (approximately)	

TABLE A22.—*Summary of results of retrospective studies of tobacco use and cancer of the larynx*

(Figures in parentheses represent ratios based on less than 5 case nonsmokers.)

Investigator reference	Relative risk ratio ¹ all smokers to nonsmokers
Schrek et al., U.S.A. (246)	2.0
Valko, Czechoslovakia (292)	3.5
Sadowsky et al., U.S.A. (232)	3.7
Blümlein, Germany (26)	27.5
Wynder et al., U.S.A. (312)	23.6
Wynder et al., India (312)	3.1
Schwartz et al., France (248)	4.6
Wynder et al., Sweden (322)	6.0
Wynder et al., Cuba (325)	(18.9) (males only)
Dutta-Choudhuri et al., India (86)	4.3
Stazewski, Poland (259)	(40.0) (males only)
Svoboda, Czechoslovakia (271)	8.3

¹ Computed according to method of Cornfield, J. (61).

TABLE A23.—*Number and percent distribution by relative frequency of atypical nuclei among true vocal cord cells, of men classified by smoking category*
(100 percent atypical cells defined as carcinoma)

Percent atypical nuclei	Current cigarette smokers											
	Never smoked regularly		Ex-cigarette smokers		Cigar/pipe smokers		Less than 1 pack a day		1-2 packs a day		2 or more packs a day	
	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent
Total	88	100.0	116	100.0	94	100.0	125	100.0	329	100.0	190	100.0
None	66	75.0	86	74.1	1	1.1	1	.8	0	—	0	—
Less than 50	8	9.1	14	12.1	4	4.3	25	20.0	4	1.2	0	—
50-59	10	11.4	13	11.2	50	53.0	54	43.2	87	26.4	29	15.3
60-69	4	4.5	1	.9	23	24.5	21	16.8	116	35.3	75	39.4
70-79	0	—	2	1.7	9	9.6	9	7.2	44	13.4	38	20.0
80-89	0	—	0	—	2	2.1	2	1.6	19	5.8	11	5.8
90-99	0	—	0	—	1	1.1	0	—	5	1.5	0	—
100:												
Carcinoma <i>in situ</i>	0	—	0	—	3	3.2	13	10.4	52	15.8	35	18.4
Invasive carcinoma	0	—	0	—	1	1.1	0	—	2	.6	2	1.1

Source: Auerbach, O. et al. (9).

TABLE A24.—*Number and percent distribution, by highest number of cell rows in the basal layer of the true vocal cord, of men classified by smoking category*

Number of cell rows	Current cigarette smokers											
	Never smoked regularly		Ex-cigarette smokers		Cigar/pipe smokers		Less than 1 pack a day		1-2 packs a day		2 or more packs a day	
	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent
Total	88	100.0	116	100.0	94	100.0	125	100.0	329	100.0	190	100.0
Less than 5 cell rows	30	34.1	7	6.0	4	4.3	3	2.4	1	0.3	0	...
5 cell rows	29	33.0	27	23.3	20	21.3	27	21.6	38	11.6	20	10.5
6 cell rows	8	9.1	15	12.9	15	6.0	25	20.0	51	15.4	24	12.6
7 cell rows	6	6.8	12	10.3	18	19.1	12	9.6	38	11.6	19	10.0
8 cell rows	8	9.1	14	12.1	9	9.6	13	10.4	30	9.1	23	12.1
9 cell rows	1	1.1	7	6.0	7	7.4	6	4.8	26	7.9	14	7.4
10 or more cell rows	6	6.8	34	29.4	21	22.3	39	31.2	145	44.1	90	47.4

Source: Auerbach, O. et al. (9).

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Cases		Number	Controls		Comments
		Number	Method of selection		Number	Method of selection	
Borders, 1920, U.S.A. (43).	M.	526	Series of clinic patients with epithelioma of the lip:	500	Series of clinic patients without epithe- lioma of the lip:		
	F.	11					
			<i>Percent</i>			<i>Percent</i>	
			Tobacco users			Tobacco users	
			Smokers			Smokers	
			Cigarettes			Cigarettes	
			Chewers			Chewers	
			Pipes			Pipes	
Ebenius, 1943, Sweden (87).	M.	439	Clinic patients with cancer of the lip:	300	Not defined.		† Estimate of prevalence of use.
	F.	33					
			<i>Percent</i>			<i>Percent</i>	
			<i>Male Female</i>			<i>Male Female</i>	
			Tobacco users			Tobacco users	
			Tobacco users (all pipes)			Tobacco users	
			Pipes			Pipes	
			Chew or use snuff			Chew or use snuff	
			Cigars and cigarettes ..			Cigars and cigarettes ..	
Levin et al., 1950, U.S.A. (169).	M.	143	Cancer Institute patients with cancer of the lip:	51	Cancer Institute patients with non-can- cer diseases of same site:		
			<i>Percent</i>			<i>Percent</i>	
			Smokers			Smokers	
			Cigarettes			Cigarettes	
			Pipes			Pipes	
			Cigars			Cigars	

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Cases		Controls		Comments
		Number	Method of selection	Number	Method of selection	
Mills and Porter, 1950, U.S.A. (186).	M.	124	Deaths from cancer of oral cavity in Cincinnati and Detroit, 1940-45 and 1942-46 respectively:	185	Sample of population of Columbus, Ohio, in same proportion of color, sex, and age as in cases:	
			<i>Percent</i>		<i>Percent</i>	
			Cigarettes only		Cigarettes only	
			Pipes, cigars, or combinations		Pipes, cigars, or combinations	
Moore et al., 1953, U.S.A. (198).	M.	112	Patients over 50 years old since 1951 with cancer of oral cavity:	38	Patients of same age groups with benign oral lesions or benign surgical conditions:	
			<i>Percent</i>		<i>Percent</i>	
			Chewers		Chewers	
			Pipes		Pipes	
Sadowsky et al., 1953, U.S.A. (232).	M.	1,136	Hospital patients with lip, oral, and pharyngeal cancer, 1938-43:	615	Patients with illness other than cancer:	
			<i>Percent</i>		<i>Percent</i>	
			Cigarettes only		Cigarettes only	
			Cigars only		Cigars only	
Sanghvi et al., 1955, India (241).	M.	657	Hospital patients with cancer of oral cavity and pharynx:	288	Hospital patients with diseases other than cancer:	Smoking is of bidis among both cases and controls.
			<i>Percent</i>		<i>Percent</i>	
			<i>Male Female</i>		<i>Male Female</i>	
			Smoke and chew		Smoke and chew	
	F.	81		112		
			Smoke only		Smoke only	
			Chew only		Chew only	
			Neither		Neither	

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Cases		Controls		Comments
		Number	Method of selection	Number	Method of selection	
Ledermann, 1955, France (162).	M.	240	Patients with cancer of oral cavity and pharynx:	62	Patients with cancer of skin, bone, and muscle:	Differences between cases and controls for both high and low alcohol intake are insignificant when smoking is controlled.
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			>20 cigarettes per day		>20 cigarettes per day	
			4.6 23.4		17.2 18.6	
Wynder et al., 1957, U.S.A. (318).	M. F.	543 116	Patients with cancer of oral cavity:	207 232	Patients with cancer of other sites and benign diseases:	
			Percent		Percent	
			Male Female		Male Female	
			Nonsmokers		Nonsmokers	
			Cigars		Cigars	
			Pipes		Pipes	
			Mixed		Mixed	
			Chew		Chew	
			Cigarettes		Cigarettes	
			>35 cigarettes per day		>35 cigarettes per day	
			>16 cigarettes per day		>16 cigarettes per day	
			3 47 20 — 11 — 8 — 17 — 57 53 29 — — 34		10 70 13 — 6 — 8 — 8 — 63 30 17 — 11	
Schwartz et al., 1957, France (248).	M.	332	Hospital patients with cancer of oral cavity and pharynx:	608	Hospital patients with non-cancer illness and accident cases, matched by age:	
			Percent		Percent	
			Nonsmokers		Nonsmokers	
			Cigarettes only		Cigarettes only	
			Pipes only		Pipes only	
			16.4 62.7 3.3		23.4 58.2 3.0	

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Number	Cases Method of selection	Number	Controls Method of selection	Comments
Wynder et al., 1957, Cuba (325).	M. F.	178 34	Hospital clinic patients with cancer of oral cavity and pharynx:	220 214	Patients in same clinics with non-malignant conditions, matched by sex and age:	
			Percent Male Female		Percent Male Female	
			Nonsmokers 4 24		Nonsmokers 16 66	
			Cigarettes		Cigarettes	
			predominantly 45 62		predominantly 45 27	
			Cigars predominantly 33 12		Cigars predominantly 22 6	
Wynder et al., 1957, Sweden (322).	M.	115	Male patients with cancer of oral cavity and pharynx:	115	Male patients in same hospital with cancer of sites other than oral, pharynx, larynx, lung, esophagus, breast:	Alcohol data significant only for hypopharynx.
			Percent		Percent	
			Cigarettes 36.5		Cigarettes 36	
			Cigars 13.0		Cigars 9	
			Pipes 12.2		Pipes 16	
			Mixed 15.7		Mixed 13	
Peacock et al., 1960, U.S.A. (210).	M. F.	25 20	Hospital patients with oral cancer:	74 72	Patients in same hospital without oral cancer and 117 male and 100 female out-patients, randomly selected.	
			Percent			
			Chewed or used snuff over 20 years (all patients) 55.6		32.6 percent of first group, and 43.3 percent of second group chewed or used snuff over 20 years.	
Staszewski, 1960, Poland (259).	M.	383	Male patients with oral cancer:	912	Male patients with other cancerous and non-cancerous conditions:	
			Percent		Percent	
			Nonsmokers 5.7		Nonsmokers 17.3	
			"Heavy" smoking index 72.8		"Heavy" smoking index 49.0	
			Cigarettes only 72.3		Cigarettes only 60.5	
			Pipes and/or cigars 12.8		Pipes and/or cigars 11.1	

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Cases		Controls		Comments
		Number	Method of selection	Number	Method of selection	
Vogler et al., 1962, U.S.A. (298).	M.	188	Clinic patients with cancer of lip and oral cavity:	521	Patients of same clinic with other cancer or non-malignant conditions:	† Due to varying tabular treatment of data, percentages of tobacco users are not all based on the same number of cases.
	F.	92		1,064		
			Percent			
			Male Female			
			Chewers	†32.9	—	
			Excessive chewers	22.9	—	
			Snuff dippers	—	72.0	
			Excessive snuff dippers	—	41.3	
			Tobacco users	90.0	90.0	
					Percent	
					Male Female	
				Snuff dippers	†6.1	
				Tobacco users	56.0 56.0	
Vincent and Marchetta, 1963, U.S.A. (297).	M.	66	Successive patients with lesions of buccal cavity and oropharynx:	100	Successive patients attending gastrointestinal clinic, age-matched:	Male patients used considerably more alcohol than male controls. Data refers to all forms of smoking expressed as cigarette equivalents. Cigarette equivalents: 1 cigar = 5 cigarettes 1 pipe = 2 cigarettes † BN=Betel nut.
	F.	16		50		
			Percent			
			Oral Oro-Cavity pharynx			
			Males:		Percent	
			Nonsmokers	3.0	—	
			<20 cigarettes per day	18.3	15.1	
			>20 cigarettes per day	78.7	84.9	
			Females:			
			Nonsmokers	55.5	28.6	
			<20 cigarettes per day	—	—	
			>20 cigarettes per day	44.5	71.4	

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Sex	Cases			Controls			Comments	
		Number	Method of selection	Number	Method of selection				
Shanta and Krishnamurthi, 1964, India (256).	M.	552	Patients with oral and pharyngeal cancer	300	Controls residing in same area matched for age, sex, and class:				
	F.	206	(unsure of confirmation):	100					
					Percent				
					Anterior	Posterior	Pharynx	Males	
					tongue	tongue			
Wahi et al., 1965, India (302).	M.	589	Patients with oral and pharyngeal carcinoma:	589	Patients matched for age, sex, religion, and social class.				
	F.	232		232					
					Percent				
Hirayama, 1966, Central and South East Asia (124).	M.	369	Patients with oral and pharyngeal carcinoma:	277	Patients with other (unspecified) diseases:			Found only a suggestive association between alcohol-drinking and oral cancer in non- chewers only. † BN-Betel nut.	
	F.	176		163					
					Percent				
					Male	Female	Male		Female

TABLE A28.—Outline of retrospective studies of tobacco use and cancer of the oral cavity (cont.)
(Data obtained from patient interview and other sources)

Author, year, country, reference	Cases			Controls		Comments
	Sex	Number	Method of selection	Number	Method of selection	
Keller, 1967, U.S.A. (140).	M.	408	Patients with squamous cell carcinoma of oral cavity and oropharynx confirmed histologically. Three New York City VA Hospitals 1953-68:	408	Next male patient admitted to same hospital within 5 year age range.	Excessive alcohol consumption noted for cases involving floor, mesopharynx, and tongue. Findings indicate the association of heavy drinking with cancer independent of the amount of tobacco used.
			<i>Percent</i>		<i>Percent</i>	
			Nonusers		14.2	
			Cigarettes		56.4 (p<0.0001)	
			Pipe only		2.9	
			Cigar only		6.1	
Martinez, 1969, Puerto Rico (188).	M.		Patients with epidermoid carcinoma of oral cavity and pharynx:	345	115 male and 38 female hospital or clinic patients without cancer; 330 male and 76 female residents of same region, age and sex matched.	Cases found to consume more alcoholic beverages than controls.
	F.	38		114		
					<i>Percent</i>	
					19.2	
			Nonsmokers		12.2 (p<0.0001)	
			Heavy tobacco users			
Keller, 1970, U.S.A. (141).	M.	304	Patients with primary basal or squamous cell carcinoma of lip:	304	Patients from same hospital matched for age and race.	
			<i>Percent</i>		<i>Percent</i>	
			Nonsmokers		16.6 (p<0.001)	
			Cigarettes only		52.8	
			Pipe only		3.4	
			Pipe, other		0.4 (p<0.01)	

TABLE A28a.—*Summary of results of retrospective studies of smoking by type and oral cancer of detailed sites*

Author reference	Cigarettes	Cigarettes and cigars	Bidis	Pipes only	Pipes and other forms	Cigars only	Tobacco chewing	Betel nut chewing	Miscellaneous
Broders (43)	Lip (—)			Lip (+)		Lip (—)	Lip (+)		
Ebenius (87)		Lip (—)		Lip (+)			Lip (—)		
Levin et al. (169)	Lip (—)			Lip (+)		Lip (*)			
Mills and Porter (186)	Oral (*)								Pipes and cigars combined—oral (+)
Moore et al. (193)		Lip, mouth (—)		Lip, mouth (—)			Lip, mouth (+)		Snuff—lip, mouth (+)
Sadowsky et al. (232)	Lip, tongue, other oral, pharynx (—)			Lip, tongue, other oral (+)		Tongue, other oral (*)			
Sanghvi et al. (241)			Oral (+)				Oral (+)		If smokers and chewers—base of tongue, hypopharynx (+)
Lederman (162)	Oral (+)								
Wynder et al. (313)	Floor of mouth Male (*) Female (+)			Each site except tongue (+)		Each site (+)	Gingiva, lip (*)		
Schwartz et al. (248)		Pharynx (+)		Oral (—)					

TABLE A28a.—Summary of results of retrospective studies of smoking by type and oral cancer of detailed sites (cont.)

Author reference	Cigarettes	Cigarettes and cigars	Bidis	Pipes only	Pipes and other forms	Cigars only	Tobacco chewing	Betel nut chewing	Miscellaneous
Wynder et al. (325)	Oral and pharynx, Male (—) Female (+)					Oral and pharynx, Male (+), Female (+)			
Wynder et al. (323)	Pharynx (+), other sites (—)					Tongue, gingiva, pharynx (+)			Pipes and cigars combined—tongue (+).
Peacock et al. (210)							Oral (+) ¹		Snuff—oral (+) ¹
Staszewski (259)	Lip, oral cavity (+)								Pipes and cigars combined—lip, oral cavity (*).
Vogler et al. (298)									All forms combined (+), Female (+) Snuff—lip and buccal cavity in both cases.
Vincent and Marchetta (297)									All forms combined—oral (+), pharynx (+).
Shanta and Krishnamurthi (256)							Lip, buccal mucosa (+)		All smoking types—pharynx (+), post tongue (+). All forms combined—lip, oral cavity, pharynx (+).

TABLE A28a.—Summary of results of retrospective studies of smoking by type and oral cancer of detailed sites (cont.)

Author reference	Cigarettes	Cigarettes and cigars	Bidis	Pipes only	Pipes and other forms	Cigars only	Tobacco chewing	Betel nut chewing	Miscellaneous
Wahi et al. (302)	Anterior tongue and buccal mucosa, Males (+)							Anterior tongue and buccal mucosa, Males (+)	All forms combined—all sites (+).
Hirayama (124)				All sites (—)		All sites (—)	All sites (—)		All forms combined—base of tongue (+), oropharynx (+). Smoking only combined—buccal mucosa (+).
Keller (140)	All sites (+)		All sites (—)			All sites (—)			All types smoking combined, heavy—floor of mouth and tongue (+).
Martinez (133)	Oral cavity, pharynx (+)								All types of smoking, heavy, combined—oral cavity (+), pharynx (+).
Keller (141)	Lip (—)				Lip (+)	Lip (—)			All types of smoking combined—lip (+).

¹ Only in individuals of low economic status and over 60 years old.

Symbols: (+) = significant association.

(—) = association absent or not significant.

(*) = association of doubtful significance.

TABLE A29.—*Experimental studies concerning oral carcinogenesis*

Author, year, country, reference	Animal and strain	A. Method. B. Frequency and/ or duration. C. Material.	Results			
Kreshover, 1952, U.S.A. (152).	78 Swiss and C57 mice.	A. Painting of lower lip mucocutaneous region. B. 10 times in 76 days. C. Cigarette smoke "concentrate".	No macroscopic or microscopic changes in controls or experimental animals.			
Salley, 1954, U.S.A. (238).	36 Syrian hamsters.	A. Painting of cheek pouch. B. 3 per week for 16 weeks. C. Benz(a) pyrene in acetone or benzene.	Treatment: Acetone solvent Benzene solvent	Number of survivors 5 4	Number with benign tumors 1 —	Number with carcinoma 2 —
Holsti and Ermala, 1955, Finland (130).	60 Albino mice (40 controls).	A. Painting of lips and oral cavity. B. 140 times in 12 months. C. Tobacco "tar".	No oral or labial changes seen in controls or experimental animals.			
Moore and Miller, 1958, U.S.A. (192).	80 Syrian Golden hamsters.	A. Material soaked onto wad and secured in cheek pouch. B. Wads replaced 8 times in 2 years. C. Smoke condensate Benz(a) pyrene.	Treatment: Controls Smoke condensate Benz(a) pyrene	Original number 30 80 20	Surviving over 1 year 23 55 16	Number tumors Inflammation and basal cell hyperplasia 4 32 9
Guerin, 1959, France (108).	Strain IC and strain W rat.	A. Chamber inhalation of tobacco smoke. B. Daily (?). C. Up to 5½ months.	Controls Experimental	Original number 40 100	Survivors 39 68	Buccal tumors 0/39 5/68 (3/5 definite epithelioma)

TABLE A29.—*Experimental studies concerning oral carcinogenesis (cont.)*

Author, year, country, reference	Animal and strain	A. Method, B. Frequency and/ or duration, C. Material.	Results				
Peacock et al., 1960, U.S.A. (210).	124 Syrian Golden hamsters.	A. Packing of cheek pouch. B. 1 year. C. Snuff, Tobacco, Bland material.	No tumors noted in any of the 42 animals surviving over 1 year.				
Dunham and Herrold, 1962, U.S.A. (84).	Syrian Golden hamsters.	A. Packing of cheek pouch. B. Normal lifespan or 5-30 months. C. Betel quid ingredients 7-12 dimethylbenz (a)- anthracene (DMBA), Methylcholanthrene (MCA) in beeswax pellets.	Treatment: Betel quid DMBA and MCA	Original number 375 71	Survivors 90% over 1 year 56/71 over 5-30 months	Hyperplasia and/or in- flammation 19 —	Malignant pouch tumors — 23/56
Moore and Christo- pherson, 1962, U.S.A. (191).	Albino hamster exteriorized oral pouch.	A. Painting oral mucosa. B. 3 per week for 683 days. C. Cigarette smoke condensate. DMBA in 0.5% petrolatum.	Treatment: Controls Smoke condensate DMBA	Animals with lesions (time) 0-18 (at 392 days). 0/20 (at 337 days) (10 showed hyper- keratosis). 14/21 microscopic cancers (at 90 days) (invasive squamous cancer originating in the skin at the edge of the pouch).			
Salley, 1963, U.S.A. (239).	CAF ₁ strain mice.	A. Ultraviolet light exposure to and painting of lips. B. 3 per week for 98 weeks. C. B(a)P in acetone Cigarette smoke UV light.	Treatment: Ultraviolet light and cigarette smoke B(a)P and UV light UV light B(a)P	Number 40 40 40 40	Duration weeks 94 48 94 45	Tumors — — — —	

TABLE A29.—*Experimental studies concerning oral carcinogenesis (cont.)*

Author, year, country, reference	Animal and strain	A. Method. B. Frequency and/ or duration. C. Material.	Results							
	Hamsters	A. Application to cheek pouch.	Treatment:	Original Number	Survivors	Duration	Lesions			
		B. See results.	Cigarettes 5 per week	70	55	64	—			
		C. See results.	DMBA once	13	6	128	2 hyperplasia			
		Croton oil 3 per week	10	10	30	—				
		DMBA once and cigarettes 5 per week	30	28	81	12 hyperplasia 4 dyskeratosis 1 carcinoma				
		DMBA once then croton oil 5 per week	29	27	81	7 hyperplasia 6 dyskeratosis 3 carcinoma				
		Bock et al., 1964, U.S.A. (30).	ICR Swiss mice.	A. Painting mouse skin.					Number tumors/ number mice	
				B. See results 36 weeks.					with tumors	
				C. Various extracts of unburned tobacco DMBA.	Treatment:				Tobacco equivalent (cigarettes/daily)	(small papillomas)
				DMBA once then:						
Acetone benzene extract					2.5	16/7				
Concentrated Ba(OH) ₂ extract					0.5	18/8				
Diluted Ba(OH) ₂ extract					0.5	6/2				
DMBA only					—	—				
Acetone benzene extract			2.5	—						
Concentrated Ba(OH) ₂ extract			0.5	—						
Diluted Ba(OH) ₂ extract			0.5	—						
None			—	—						

TABLE A29.—*Experimental studies concerning oral carcinogenesis (cont.)*

Author, year, country, reference	Animal and strain	A. Method. B. Frequency and/ or duration. C. Material.	Results							
Protzel et al., 1964, U.S.A. (213).	Swiss Webster mice with some having liver damage in- duced either by CCl4 or ethyl alcohol.	A. Swabbing of labial mucosa.				Original number	Percent at 13 months with Papillomas		Cancer	
		B. Up to 13 months.	Alcohol and CCl ₄ treated			40	74	46		
		C. B(a)P in acetone.	Alcohol treated			40	84	50		
			CCl ₄ treated			40	90	40		
			No toxin			40	42	15		
Reddy and Anguli, 1967, India (219).	Swiss female mice.	A. Intravaginal instillation.				Original number 60	Survivors 40	Lesions		
		B. Daily for 324-380 days.						3/40 raised papillomatous malignant growths		
		C. "Pan" mixture of areca nuts, lime, and chewing tobacco.						4/40 possible carcinoma- in situ.		
Elzay, 1969, U.S.A. (90).	Syrian Golden hamsters.	A. Application to cheek pouch.				Original number	Mortality rate	Number animals	Percent with tumors	Percent with cancer
		B. Daily for 200 days.	Treatment:							
		C. See results.	DMBA	Alcohol	Smoke	29	41.0	17	100.0	50.0
			DMBA	Alcohol	29	66.0	10	60.0	40.0
			DMBA	Smoke	29	42.0	14	100.0	70.0
			DMBA	29	48.0	15	100.0	38.0
			Alcohol	Smoke	29	42.0	14	—	—
			Smoke	29	42.0	14	—	—

TABLE A31.—*Summary of methods used in retrospective studies of tobacco use and cancer of the esophagus*

Author, year, country, reference	Cases			Controls		Collection of data
	Sex	Number	Method of selection	Number	Method of selection	
Sadowsky et al., 1953, U.S.A. (252).	M.	104	White patients admitted during 1938-43 to selected hospitals in New York City, Missouri, New Orleans, and Chicago.	615	White patients with illnesses other than cancer admitted to same group of hospitals during same period.	Obtained by 4 specially trained lay interviewers. 242 records out of a total of 2,847 excluded because of incomplete or questionable smoking histories.
Sanghvi et al., 1955, India (241).	M.	73	Consecutive clinic admissions to Tata memorial Hospital, Bombay.	288	Consecutive clinic admissions of patients without cancer.	By means of "detailed questionnaire." No other details given.
				107	Consecutive admissions of patients with cancers other than intraoral or esophagus.	
Wynder et al., 1957, Sweden (322).	M.	39	Patients admitted to Radiumhemmet, Stockholm, during 1952-55.	115	Patients admitted to same hospital with cancer of skin, head and neck region other than squamous cell cancer, leukemia, colon, and other sites. No matching.	
	F.	35		156		
Staszewski, 1960, Poland (260).	M.	24	Patients admitted to Oncological Institute during 1957-59.	912	Other patients sent to Institute with symptoms probably not etiologically connected either with smoking or with diseases of esophagus, stomach or duodenum.	No details given on method of data collection. No age adjustment or matching. Average age of cancer patients, 60.5; controls, 53.